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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,577	WAISMAN, DAVID M.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-45* is/are pending in the application.

4a) Of the above claim(s) *7,9-16 and 19-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6,8,17,18 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection not reiterated in this Action is withdrawn.

Status of the application

Claims 1, 3 and 5-45 are pending in the application. Claims 1, 3, 5, 6, 8, 17, 18 and 45 are examined on the merits.

Claims 7, 9-16 and 19-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 25, 2005. It is noted that claim 7 was inadvertently included in the rejections of record, however this claim is directed to antisense sequences other than the elected sequence and is withdrawn as being a non-elected invention. The examiner regrets any confusion over the inclusion of this claim.

Claim Objections

Claims 5, 6 and 8 are objected to because of the following informalities: claims 5 and 6 contain non-elected subject matter, specifically the non-elected antisense sequences. Claim 8 depends from a withdrawn claim. For the purposes of examination this claim has been assumed to depend from claim 6. Appropriate correction is required.

Claims 6 and 8 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Because the application has been restricted to a single antisense sequence, the scope of claims 6 and 8 are identical to that of claim 5, a sequence of SEQ ID NO: 16.

Applicant is advised that should claim 1 be found allowable, claim 45 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 1 and 45 are directed to the same subject matter, compositions comprising an antisense p11 polynucleotide and a pharmaceutically acceptable carrier. The different intended uses of these compositions recited in the preamble do not distinguish the components of the compositions themselves, which are the same.

Claim Rejections - 35 USC § 112

Claims 1, 3, 17 and 18 remain rejected under 35 U.S.C. 112, first paragraph and new claim 45 is rejected as failing to comply with the written description requirement for the reasons set forth in the office action mailed October 3, 2005 and reiterated below.

Claims 1 and 45 are directed to a composition of an antisense p11 polynucleotide that modulates activity of an extracellular p11 protein and affects a change in either the level of plasminogen activation by a cell or the level of tumor growth, invasiveness and metastasis. Claims 1 and 45 encompass any antisense polynucleotide that modulates activity of any extracellular p11 protein from any species. Claim 3 limits claim 1 by stating the composition inhibits the production of the p11 protein by the cell. Claims 17 and 18 limit claim 1 by stating the cell is a cancer cell that may be one of several recited types of cancer.

The specification describes compositions that modulate activity of p11 as including antisense and sense p11 polynucleotides, siRNAs specific to p11, inhibitory antibodies, p11-receptor blocking peptides, p11 antagonists and agonists and soluble fragments of the p11 protein receptor. The specification discloses several antisense polynucleotides and siRNAs and one sense polynucleotide, presumably directed to human p11.

The specification does not describe the structure of nucleic acid modulators to a p11 protein from a species other than the p11 targeted in the working examples (presumably human) that correspond to the function of modulating p11 and plasminogen activation in a cell.

In order for the written description provision of 35 USC 112, first paragraph to be satisfied, applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is,

for purposes of the 'written description' inquiry, whatever is now claimed. For example, MPEP 2163 states in part,

> "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."

The skilled artisan cannot envision the detailed structure of the encompassed antisense polynucleotides that modulate p11 from any species, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

Therefore, while the specification provides adequate description of the antisense, sense and siRNA nucleic acid modulators targeted to the p11 described in the working examples, the full breadth of antisense p11 polynucleotides from any species encompassed by the claims do not meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

Response to arguments: Claim Rejections - 35 USC § 112

Applicant's amendment of claim 1 has overcome the aspects of the written description rejection directed to the type of p11 modulators. The aspects of the

rejection directed to the structure of antisense polynucleotides directed to p11 from any species are maintained as described above.

Applicant argues that the specification provides a representative number of species of p11 protein and antisense polynucleotides to support the claimed genus. In support of this argument applicant points to page 23 of the specification describing how the primary structures of p11 are conserved among vertebrates. Applicant further points to the definition of an antisense polynucleotide as complementary to a p11 RNA that can be translated to produce a p11 polypeptide or a fragment thereof. These arguments are not persuasive because the claims are not limited to antisense polynucleotides to vertebrate p11. Also, the similarity of p11 among vertebrate species cited in the specification refers to the protein primary sequence, not the nucleic acid sequences that encode these proteins. Nucleic acids that encode proteins having only 61% identity, as with p11 from human and xenopus, can be quite different. An antisense polynucleotide to one of these nucleic acids would not lead the skilled artisan to the structure of an antisense polynucleotide targeted to portions of the nucleic acids that are not identical. Therefore, the disclosure in the specification of several antisense polynucleotides targeted to the nucleic acids encoding the p11 protein of one species does not provide an adequate written description for antisense p11 polynucleotides of any other species.

Response to arguments: Claim Rejections - 35 USC § 102

Claims 1, 3, 17 and 18 remain rejected and new claim 45 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yao et al. for the reasons set forth in the office action mailed October 3, 2005.

Applicant traverses the rejection over Yao et al. by arguing that the focus of the Yao et al. reference was the study of cytosolic phospholipase A_2 activity and Yao et al. does not disclose or suggest a composition that can modulate the activity of an extracellular p11 protein or that their p11 antisense mRNA modulates plasminogen activation as required by claim 1. Based on these arguments applicant concludes that the Yao et al. reference does not describe every element of the claim and therefore does not anticipate the instantly claimed invention. The examiner acknowledges applicant's clarification that plasminogen activation is a cell surface event, however, these arguments are not persuasive because the claimed invention is a composition comprising an antisense p11 polynucleotide but the arguments are directed to both Yao et al.'s and applicant's intended use of the composition. Claim 1 is directed to an antisense p11 polynucleotide and Yao et al. disclose an antisense p11 polynucleotide. Since the structural limitations are met, then absent evidence to the contrary the claimed function also exists.

Applicant further argues that the antisense polynucleotide disclosed by Yao et al. does not meet the structural limitations of the claims because nowhere in the reference is it disclosed that the polynucleotide is isolated or in combination with a pharmaceutically acceptable carrier. This argument is not persuasive because the Yao

et al. reference discloses that the plasmid, which is an isolated polynucleotide comprising an antisense p11 polynucleotide, is delivered as a composition comprising lipofectamine, which is a pharmaceutically acceptable carrier.

Applicant argues that the office has not met its burden of proof for an inherency rejection of claim 1. As a support for this argument applicant cites the use by Yao et al. of an antisense p11 polynucleotide to inhibit cellular p11 protein. Based on the use of the prior art polynucleotide for a purpose different from applicant's intended use, applicant concludes that one skilled in the art would not expect the polynucleotide disclosed by Yao et al. would result in a change in the level of extracellular plasminogen activation. Applicant further argues that the Office has not shown that the antisense p11 polynucleotide disclosed by Yao et al. would necessarily work in an extracellular environment to modulate plasminogen levels.

In response to the arguments regarding the office's burden of proof for an inherency rejection, applicant's arguments are not persuasive because the office is not required to show that the polynucleotide of Yao et al. would result in a change in plasminogen activation. As stated in MPEP 2112:

> V. ONCE A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE
>
> "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on '*prima facie* obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Since applicant has not provided evidence to demonstrate that the antisense p11 polynucleotide disclosed by Yao et al. in combination with a pharmaceutically acceptable carrier does not change the level of plasminogen activation by a cell, the rejection under 35 USC 102(b) is maintained as proper.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 5, 6, 8, 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Mehta et al. (US 6,841,539).

The claims are directed to compositions of antisense p11 polynucleotides. Claims 5, 6 and 8 are directed to a composition comprising a sequence as set forth in SEQ ID NO: 16. For the purposes of prior art, claims reciting "a sequence" are interpreted to encompass SEQ ID NO: 16 or any portion of this sequence. A portion of the claimed sequence can have as few as two nucleotides in common with SEQ ID NO: 16. Change of the word "a" to "the" will change the scope of the claim to encompass only full length SEQ ID NO: 16.

Mehta et al. disclose an antisense oligonucleotide designated as SEQ ID NO: 5 that shares 11 of 21 nucleotides within nucleotides 73-93 of SEQ ID NO: 16. Mehta et al. disclose at columns 5-15 pharmaceutically acceptable carrier for the formulation of compositions comprising the oligonucleotides of the invention. Although Mehta et al. do not disclose that their oligonucleotides is an antisense p11 polynucleotide or that this oligonucleotide affects a change of plasminogen activation by a cell, the oligonucleotide meets the structural limitations of the claims and would be expected to have this function, absent evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The central FAX Number is 571-273-8300.

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Tracy Vivlemore
Examiner
Art Unit 1635

TV
July 7, 2006

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER